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U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional)	
1959-7467.1US (N-405US-DIV)	

Application Number	Filed
10/614,344	July 8, 2003

NOTICE OF EXPRESS MAILING

Express Mail Mailing Label Number: EL995985191US

Date of Deposit with USPS: February 13, 2007

Person making Deposit: Diane M. Sanders

First Named Inventor: Artman et al.

Art Unit	Examiner
1617	D. Claytor

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [X] attorney or agent of record. Registration number 39,931.
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Signature

Edgar R. Cataxinos

Typed or printed name

801-532-1922

Telephone number

February 13, 2007

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of _____ forms are submitted.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Artman et. al.

Serial No.: 10/614,344

Filed: July 8, 2003

For: TREATING A VARIETY OF PATHOLOGICAL CONDITIONS, INCLUDING SPASTICITY AND CONVULSIONS, BY EFFECTING A MODULATION OF CNS ACTIVITY WITH ISOVALERAMIDE, ISOVALERIC ACID, OR A RELATED COMPOUND

Confirmation No.: 7848

Examiner: D. Claytor

Group Art Unit: 1617

Attorney Docket No.: 1959-7467.1US
(N-405US-DIV)

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PRE-APPEAL BRIEF

MAIL STOP AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Pre-Appeal Brief is submitted pursuant to the U.S. Patent and Trademark Office OG Notices of 12 July 2005 regarding the Pre-Appeal Brief Pilot Program. Applicant respectfully submits that the outstanding rejections of record clearly are not proper and are without basis. As set forth below, there is a clear factual deficiency in the rejections.

Independent claims 37 and 39 are pending in the present application. Claim 37 is directed to a method of treating a convulsive disorder in a patient comprising administering an effective amount of isovaleramide to a patient suffering from a convulsive disorder, wherein the convulsive disorder is selected from the group consisting of simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, and trauma-induced seizures. Independent claim 39 is directed to a method of treating headaches in a patient comprising administering an effective amount of isovaleramide to a patient suffering from headaches. The outstanding rejections of record are as follows:

1. Claim 37 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Balandrin et al. (U.S. Patent No. 5,506,268) in view of Drug Facts and Comparisons, 1999 Ed., Pages 1595-1597 ("Drug Facts"); and

2. Claim 39 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Balandrin et al. (U.S. Patent No. 5,506,268) in view of Pharmacotheraphy, A Pathophysiologic Appropach (Dipiro et al., 2nd Ed., Elsvier, 1991, Pages 1232, 1238) ("Pharmacotherapy").

Brief Background of the Technology

A number of pathological states, diseases, and disorders are characterized by a profound aberration in the normal function of the central nervous system (CNS). At the clinical level, these states usually only respond to pharmacologic intervention with compounds or substances that possess significant activity at the level of the CNS.

Many agents currently employed in the treatment of pathologies such as spasticity and convulsions display troubling side-effect profiles which limit their long-term clinical utility. Among these agents, for example, are the benzodiazepines, which can cause impairment of cognition (impairment of memory-related performance, or "cognitive blunting"). Two other clinically used agents are valproate and related therapeutically useful salts such as valproic acid hemisodium salt, which are hepatotoxic and teratogenic, and baclofen, which produces excessive muscle weakness and sedation. These side-effects severely limit the therapeutic potential for both drugs. It is apparent, therefore, that improved and better-tolerated treatments for spasticity, convulsions, and other therapeutic indications are greatly to be desired.

Accordingly, the present invention provides a therapeutic approach for the treatment of various pathologies by effecting a modulation of CNS activity without producing excessive sedation, muscle weakness, fatigue, teratogenicity or hepatotoxicity. The present invention provides methods of treating pathological conditions, such as spasticity and convulsions, the symptoms of which are alleviated by a modulation of activity in the central nervous system (CNS), without producing undesirable excessive sedation or muscle weakness in animal subjects, including humans. More particularly, the invention relates to the therapeutic use of isovalerarnide in patients suffering from simple partial seizures, complex partial seizures, generalized tonic-clonic seizures, secondarily generalized seizures, status epilepticus, trauma-induced seizures, and headaches.

Arguments

Applicant respectfully asserts that the Examiner has clearly failed to provide a factual basis sufficient to support any one of the outstanding rejections of record. The Examiner has asserted that, while Balandrin et al. does not teach the use of isovaleramide for the convulsive disorders recited in claim 37, Drug Facts teaches that diazepam "is an anxiolytic that is a muscle relaxant and an anti-convulsant to treat status epillepticus and recurrent convulsive seizure." As such, the Examiner concludes that a person of skill "would have been motivated to use isovaleramide as a treatment for convulsive disorders, including status epilepticus, because another anxiolytic (diazepam) has been used as a muscle relaxant and an anti-convulsant." (Final Office Action at pg. 5).

While Balandrin teaches that valproic acid and valpromide are used as antiepileptic agents, Balandrin explicitly states that isovaleramide has no anticonvulsant properties. (Balandrin, Col. 4, lines 60-65). Balandrin also explicitly states "that there are no clearly discernible structure-function relationships which permit predictability of compounds which will affect the central nervous system in the experimentally distinguishable outcomes described herein below." (*Id.* at column 4, line 66 through column 5, line 3).

Contrary to the Examiner's arguments, nothing in Balandrin teaches or suggests that isovaleramide has antispasmodic effects. While Balandrin teaches that valerian extracts have

antispasmodic effects, it is improper for the Examiner to rely on this teaching in support of the assertion that isovaleramide has antispasmodic effects, especially since Balandrin teaches that the active components in the valerian extracts have not been identified, nor have the effects of the active components been characterized. Furthermore, even assuming *arguendo* that the Examiner's argument is correct, the above-mentioned limitation still is not taught or suggested because Balandrin does not teach or suggest the specific convulsive disorders recited in claim 37.

Drug Facts has been cited "to show that for the purposes of treating the conditions of anxiety disorders, muscle spasms and convulsive disorders such as status epilepticus, one of ordinary skill in the art would have viewed said conditions to be art equivalents" and that "one of ordinary skill in the art would have expected to see therapeutic benefits for treating all such conditions, when any agent is found to be effective to treat any one of said conditions." (Final Office Action at pg. 3) (emphasis added) However, Drug Facts does not recite, teach or suggest use of isovaleramide.

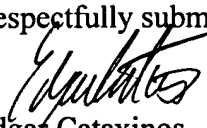
With regard to the Examiner's reliance on Drug Facts, Applicants respectfully disagree that Diazepam, which is a benzodiazepine compound having an entirely different chemical structure than isovaleramide and having a different mechanism of action, somehow provides evidence that treating the conditions of anxiety disorders, muscle spasms and convulsive disorders such as status epilepticus is viewed by a skilled artisan as being an art equivalent to the conditions recited in claim 37. There is also no support for the contention that one of ordinary skill in the art would have expected to see therapeutic benefits for treating all such conditions, when any agent is found to be effective to treat any one of said conditions. Given the different chemical structure of Diazepam and isovaleramide, as well as the differences in mechanisms of action, such a conclusion is unsupportable. Applicants respectfully submit that nothing in Balandrin teaches or suggests administering isovaleramide to a patient suffering from a convulsive disorder, instead being limited to teaching its use as an anxiolytic or sedative. Therefore, Balandrin, either alone or in combination with Drug Facts, does not teach or suggest that the convulsive disorders recited in claim 37. The cited references also do not provide a reasonable expectation of success. In addition, the cited references do not provide a motivation to combine to produce the claimed invention.

With regard to claim 39, the Examiner has further asserted that, while Balandrin et al. does not teach the use of isovaleramide to treat a headache, the claim would have been obvious because "Pharmacotherapy teaches that headache is a common symptom associated with premenstrual syndrome," and "headache is a common symptom of [premenstrual syndrome]." (Final Office Action at pg. 6).

As acknowledged by the Examiner, Balandrin does not disclose that isovaleramide treats headache. Likewise, reliance on Pharmacotherapy is misplaced. There is no support for the theory that PMS symptoms and headaches are interchangeable or that there is any expectation of success for treating headaches simply because one particular benzodiazepine compound (alprazolam) is effective for treating one or more PMS-related symptoms. Pharmacotherapy recites over 80 symptoms that are associated with PMS. (Pharmacotherapy at page 1232; Table 72.1). It also recites a myriad of therapeutic compounds that have been tried as possible treatments for the numerous symptoms associated with PMS. (*Id.* at pages 1237-1238). The mere listing of numerous possible compounds having potential to treat a myriad of PMS symptoms does not overcome the deficiencies of Balandrin.

As the Examiner has failed to properly identify any description, teaching, or suggestion in the cited references of each and every element recited in claims 37 and 39, Applicants respectfully assert that the outstanding rejections of record are factually deficient and should not be maintained.

Respectfully submitted,



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